to a positive balance of approximately 1.4 mg. daily in the male, which is quite enough to account for deposits of this magnitude.

In females the findings were very different, since about 75% had iron concentrations in the liver which were normal or very close to normal, and although severe siderosis did occur it was uncommon. Of the whole group, nine had between 5 and 10 g. in the liver while only two had more than 10 g. The much lower incidence of iron overload is possibly explicable on the greater physiological losses which occur in females. It has been calculated that the average female loses up to 10 g. of iron through menstruation, pregnancies, and lactation during the reproductive period of life (Finch and Finch, 1955). On this basis it might be anticipated that the incidence and severity of iron overload would be less in females. Whether this is the only factor is, however, open to question. There is good evidence that the major source of iron in the Bantu diet is "kaffir beer" (Walker and Arvidsson, 1953), and females, on the whole, tend to drink less of this than do males. It is thus probable that the majority ingest less iron than do males.

The well-marked association between severe hepatic siderosis and significant portal fibrosis or actual portal cirrhosis, which has been noted in previous studies, was confirmed in the present investigation. This association was most striking with iron concentrations above 2% dry weight. The frequency with which such pathological changes develop in the siderotic liver suggests that they are the direct result of the iron deposits. However, it is perhaps noteworthy that 10 of the 35 subjects who were over the age of 50 and who had iron concentrations above 2% dry weight showed no significant portal fibrosis. Discrepancies such as this underline the complexity of the problem and suggest that other as yet unidentified factors may be involved. It has been shown experimentally that the liver overloaded with iron is very vulnerable to toxic, nutritional, and metabolic hazards (Golberg and Smith, 1960), and it is possible that such factors may also potentiate the effects of iron deposits in the Bantu.

Whatever the exact relationship between iron overload and hepatic fibrosis there is no doubt that a proportion of subjects end up with histological findings in the liver which are indistinguishable from those in idiopathic haemochromatosis. The results of a previous study indicate that cases with severe siderosis and portal cirrhosis invariably have significant epithelial deposits elsewhere in the body (Isaacson *et al.*, 1961). These are particularly striking in the pancreas, and over 20% of such subjects have diabetes. It is therefore apparent that some Bantu do eventually develop both clinical and pathological findings very similar to those in idiopathic haemochromatosis. If those cases showing hepatic siderosis together with portal cirrhosis in the present study are regarded as examples of this entity, then the incidence of full-blown haemochromatosis in Bantu subjects coming to necropsy in Johannesburg is approximately 4% in males and 2% in females.

Summary

The concentration of iron in the livers of 318 Bantu males and 265 Bantu females dying in a Johannesburg hospital were estimated chemically. Of the Bantu males, 70% had significant hepatic siderosis, and in half of these subjects it was severe. In contrast 75% of

females had iron concentrations in the liver which were within or just above the normal range.

Portal fibrosis or portal cirrhosis was present in the majority of subjects with hepatic iron concentrations above 2% dry weight. The fact that this was not invariably so suggests that there are other factors which potentiate the fibrogenic effects of excessive iron deposits.

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INCIDENCE OF GENERAL PARALYSIS OF THE INSANE

BY

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In the decade 1940–9 the V.D. clinics of England and Wales diagnosed early syphilis in 100,079 individuals (Ministry of Health, 1960). With only a few exceptions these were civilian patients, and if Service cases and undiagnosed infections are added a huge potential pool for later neurosyphilis was thus created. The usual difficulties in persuading patients to undergo complete treatment with the long courses of arsenical and bismuth injections were intensified by wartime exigencies and the epidemics of hepatitis. The increasing use of penicillin from 1944 introduced new problems; initial shortage of supply, varying composition of the penicillin available, and the uncertainty of what constituted adequate treatment all contributed to the anxieties of venereologists. They were fully alive to the danger that subcurative treatment of early cases might be followed by neurosyphilis (Pick, 1946).

Harris (1958) and Mayer-Gross (1958) suggested that an increased incidence of taboparesis might be imminent. Steel (1960) and Goody, Gautier-Smith, and Dunkley (1960) reported that 18 cases of general paralysis of the insane (G.P.I.) had been admitted to a psychiatric observation ward in London between April, 1957, and September, 1958. Bockner and Coltart (1961) diagnosed nine cases of G.P.I. out of 447 patients admitted in 1959 to another psychiatric observation ward in London and suggested that the incidence of G.P.I. was increasing owing to syphilitic infections

acquired during the 1939-45 war. As the peak incidence of early syphilitic infections occurred 15 years ago, in 1946, it seemed appropriate to carry out a broadly based inquiry into the recent incidence of G.P.I., and the results are reported below.

Present Inquiry and Results

The Manchester Regional Hospital Board area* has five major mental hospitals and 16 psychiatric units in general hospitals. The psychiatrists concerned and four neurological units were asked to report the number of cases of G.P.I. seen annually between 1951 and 1960 inclusive. For various reasons data for the whole decade could be supplied by only 10 of the 16 psychiatric units in general hospitals (Table I). A more detailed inquiry into neurosyphilis was made in the four V.D. clinics in Manchester and in the 16 peripheral V.D. clinics.

Table I shows that 700 cases of symptomatic G.P.I. were diagnosed during 1951-60. The number in the last five years (329) was 42 fewer than that for the first five

TABLE I

	1951	1952	1953	1954	1955	1956	1957	1958	1959	1960	
<i>Cases of G.P.I.</i>											
5 major mental hospitals ..	38	32	33	16	23	25	19	24	24	17	251
10 psychiatric units in general hospitals ..	13	16	10	20	6	18	20	17	16	12	148
4 neurological units in general hospitals ..	9	15	14	9	13	10	6	4	5	6	91
20 V.D. clinics ..	20	17	22	19	26	26	13	24	27	16	210
Total ..	80	80	79	64	68	79	58	69	72	51	700

Cases of Neurosyphilis (excluding G.P.I.) with Paretic Curve

Taboparesis at 20 V.D. clinics ..	9	14	20	25	15	13	15	10	11	8	140
Meningovascular syphilis or optic atrophy with paretic curve ..	21	16	17	16	5	5	10	8	6	4	108
Asymptomatic neurosyphilis with paretic curve ..	16	6	8	7	4	7	6	1	4	2	61
Total ..	46	36	45	48	24	25	31	19	21	14	309

Cases of Neurosyphilis with Paretic Curve

Total ..	126	116	124	112	92	104	89	88	93	65	1,009
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years (371) of the decade (Table II). Table I also shows that the V.D. clinics, excluding symptomatic G.P.I. patients, saw 309 neurosyphilis cases with a paretic curve in the C.S.F. The annual incidence of these neurosyphilis cases shows a marked reduction in the years 1958-60. The combined totals show that 1,009 neurosyphilis cases had a paretic curve in the C.S.F.; of these, the number diagnosed in the last five years (439) was 131 fewer than that for the first five years (570) of the decade.

Discussion

While the clinical recognition of G.P.I. may be easy or difficult, laboratory confirmation of the diagnosis by examination of blood and C.S.F. is straightforward and absolute. A positive reagin test (W.R., etc.) in the C.S.F. combined with pleocytosis, increase in globulin and total protein, and the typical paretic type of Lange curve means neurosyphilis and indicates that the patient, in the absence of active treatment, is at least a potential case of G.P.I. In a patient with deterioration in memory, personality, and habits, and with disorienta-

tion, the diagnosis of G.P.I. is established. In G.P.I. the reagin tests (W.R., etc.) on the serum are positive in virtually all cases, provided the tests are sensitive and correctly carried out, and thus serological tests for syphilis should be routine in all psychiatric patients.

The clinical presentation of G.P.I. varies considerably and diagnosis may fall to general physician, geriatrician, neurologist, psychiatrist, or venereologist. It was not practicable to include general physicians and geriatricians in the inquiry, but in the Manchester Region there is good liaison between the venereologist and his other consultant colleagues, and many neurosyphilis cases reach the venereologist after diagnosis and initial treatment in another department. So far as is possible "double-reporting" of cases has been avoided in this study. It is therefore felt that the inquiry has been extensive enough to show reliably the trend in incidence.

The present study reveals no increase in the incidence of G.P.I. in the Manchester area (Table I). Except for a definite reduction in 1960 (51 cases) the annual figures have fluctuated only between 80 and 58. However, the number in the last five years (329) of the decade is 42 smaller than that (371) for the first five years (Table II).

TABLE II.—Cases of G.P.I. Diagnosed

	1951-5	1956-60
5 major mental hospitals ..	142 (38.3%)	109 (33.1%)
10 psychiatric units in general hospitals ..	65 (17.5%)	83 (25.2%)
4 neurological units in general hospitals ..	60 (18.8%)	31 (9.7%)
20 V.D. clinics ..	104 (28.0%)	106 (32.2%)
Total ..	371 (100%)	329 (100%)

The experience of the 20 V.D. clinics with neurosyphilis cases with a paretic type of Lange curve, *excluding* symptomatic G.P.I. patients (Table I), is also encouraging. Total neurosyphilis cases with a paretic curve in the C.S.F. also shows a definite reduction in 1960.

Psychiatric units in general hospitals have been expanded in the past decade and may now perhaps be seeing a greater proportion of G.P.I. cases: Table II shows that the psychiatric units in general hospitals saw 17.5% (65 out of 371) of the G.P.I. cases diagnosed in the years 1951-5 and 25.2% (83 out of 329) in the years 1956-60. This shift in the place of diagnosis may be general and would explain why psychiatrists working in general hospitals are meeting with more cases of G.P.I. (Steel, 1960; Bockner and Coltart, 1961) in spite of there being no increase in the overall total.

Although the inquiry in the Manchester area does not support the suggestion that the incidence of G.P.I. is increasing, it underlines that such cases continue to develop. Thus G.P.I. should still be kept very much in mind in differential diagnosis; when incidence is declining, diagnostic sins of omission become increasingly common. The acute confusional case should be recognized speedily, but unfortunately some present with depression, and in these the specific cause may be overlooked for many months, during which the opportunity for successful treatment is lost.

The time of onset of clinical manifestations of G.P.I. after initial infection is variable and may exceed 15 years. The figures for 1960 (Table I), however, are much lower than those for the earlier years of the decade and encourage the hope that the late harvest of neurosyphilis which many feared would follow the high rate

*Estimated home population of 4,395,000 on June 30, 1959, of whom 2,857,000 were aged 15-64 years.

of wartime infection may not result after all. If this hope proves well founded, it will represent a solid achievement for penicillin and the venereologist. The latter, however, may well wonder how much his colleagues in hospital and general practice have unwittingly helped in this happy achievement by the liberal use of penicillin for other conditions.

Summary

It was feared that the large wartime increase in syphilitic infections, which reached a peak in 1946, might result in a large aftermath of neurosyphilis, and Bockner and Coltart (1961) suggested that cases of general paralysis of the insane were on the increase.

The numbers of cases of G.P.I. diagnosed annually from 1951 to 1960 in five major mental hospitals, 10 psychiatric units in general hospitals, four neurological units, and 20 V.D. clinics situated in the Manchester Regional Hospital Board area do not support this suggestion. Of a total of 700 cases, 371 were diagnosed during 1951-5 and 329 during 1956-60; the number diagnosed in 1960 (51) was smaller than in any previous year of the decade.

I thank my consultant colleagues in psychiatry, neurology, and venereology throughout the Manchester Regional Hospital Board area for their co-operation in making this inquiry possible.

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Medical Memoranda

Maternal Death Due to Acute Adrenal Failure and Myocarditis

A search through the literature revealed only 49 cases of adrenal failure during pregnancy, the main contributors being Dewhurst (1951), MacGillivray (1951), Crawford (1951), and Barry, Meagher, and Geoghegan (1956). Of this total only three survived (Tennant and Macnaughton, 1959; Grubb, Holmes, Pearson, and Syme, 1960; Moore and Fleming, 1958) and all were given intravenous hydrocortisone, to which their survival could probably be attributed. We report a further fatal case of adrenal failure complicated by myocarditis occurring during pregnancy.

The features of the syndrome as reported are: pain in the loins associated with vomiting, cyanosis, hypotension with initially warm extremities, and normal orientation followed by shock and death; and occurring in the second half of pregnancy.

CASE REPORT

The patient, aged 31 and gravida-4, was admitted with a two-day history of vomiting, backache, dysuria, wheezing, and the coughing up of yellow sputum. She was a known asthmatic controlled with an inhaler containing "rybarvin" and tablets of "franol" three in the morning and two at night. For the 48 hours prior to admission she had been taking "franol" tablets, two every four hours. So far as was known she had never had treatment with corticosteroids.

Her L.M.P. was July 22, 1959, and the E.D.D. was April 29, 1960. She was last seen in the antenatal clinic on March 30, one week before admission, and the findings then were normal.

When examined on admission on April 5 she was dehydrated and was retching continually and coughing up yellow sputum. The blood-pressure was 110/85 mm. Hg. The jugular venous pressure was slightly raised. The pulse rate was 160 and regular. The heart sounds were normal. There was no peripheral oedema. She was wheezing, and rhonchi and crepitations were audible throughout the chest. The uterus corresponded in size to a 36-week gestation, the foetus was a vertex presentation, and there was no evidence of contractions. It was thought that the foetal heart was heard, but this was not confirmed. The patient was tender in both loins, the right more so than the left. The urine was strongly positive for acetone but otherwise normal.

An intravenous infusion of 5% dextrose in water was set up and sulphadimidine 1 g. six-hourly by intramuscular injection was started, as it was felt that she was most probably suffering from a urinary infection. Three hours after admission the pulse rate had dropped to 90 and her general condition had improved. Next morning she was found severely shocked, cyanosed, and dyspnoeic. The blood-pressure was 60/50 mm. Hg, the pulse rate was 160, and scattered crepitations were heard throughout the chest. The foetal heart was not heard. The treatment then instituted was as follows: (1) Noradrenaline ("levophed") was added to the intravenous infusion and the systolic blood-pressure rose to 90; it was maintained at this level until her death. (2) Digoxin 0.25 mg. was given intravenously. (3) Crystalline penicillin 500,000 units and streptomycin 1 g. was given intravenously.

At 11 a.m. labour began spontaneously and at 4 p.m. she was delivered of a stillborn slightly macerated female infant, weighing 8 lb. 2 oz. (3,685 g.), by low forceps extraction. From then her condition slowly deteriorated. She was given 50 mg. of hydrocortisone intravenously, but died in congestive cardiac failure at 2 a.m. on April 7.

Investigations gave the following results. Urine: a trace of albumin; microscopic examination was normal and culture sterile. Blood sugar: 48 mg./100 ml. at midday on April 6. E.C.G. at 11 a.m. on April 6 showed a sinus rhythm, rate 160 and ventricular extrasystoles.

Post-mortem Report.—The body was that of a pale cyanosed female. The heart weighed 18 oz. (510 g.). Both ventricles were hypertrophied, especially the right; the myocardium was oedematous; the valves were normal. Microscopically there was severe cloudy swelling, oedema, hypertrophy, and acute inflammatory infiltration of the myocardium. The lungs were emphysematous and showed mucopurulent bronchitis and red induration. Microscopically there were mucous plugs in the bronchi and evidence of acute interstitial inflammation in both lungs. The adrenals, which were slightly hypertrophied, showed haemorrhagic infarction. Microscopically, thrombosis was present in small veins throughout the glands. The pituitary gland showed physiological hyperplasia.

DISCUSSION

The patient showed most of the features of the syndrome described, and the differential diagnosis in a case like this would in our opinion be: (1) Pyelitis of pregnancy; an initial attack late in pregnancy is unusual, but otherwise the clinical picture would be very similar. (2) Cortisone-withdrawal syndrome would produce an identical clinical picture; there was no history of previous treatment with corticosteroids. (3) Acute pancreatitis could be ruled out by the absence of abdominal signs. (4) Cardiovascular catastrophe such as myocardial infarction or myocarditis; the latter was in fact present and was the cause of some of the symptoms. (5) Acute toxæmia of pregnancy should always be thought of in a pregnant patient. (6) Diabetic coma: